3. The evidence as to the Wassermann reaction all goes to show the unreliability of the test at this age.

4. The Lange gold chloride reaction on the cerebrospinal fluid offers at present some hope that the evidence obtained in this way may be of distinct benefit.

5. So far as we may judge from the luetin test as at present reported active treatment with mercury materially influences it, so much so that without the mercurial treatments no cases have as yet proved positive. It may be said, however, that the Noguchi test has a distinctly negative value, inasmuch as in all cases not syphilitic the reaction was negative.

MODERN METHODS OF TREATMENT OF SYPHILIS OF THE NERVOUS SYSTEM.

By B. Sachs, I. Strauss, and D. J. Kaliski,
NEW YORK CITY, N. Y.

(From the Neurological Service and the Pathological Laboratory of the Mount Sinai Hospital, New York.)

The discoveries of Schaudinn, Wassermann, Ehrlich, and Noguchi have led to great changes in the methods of diagnosis and of treatment of syphilitic disease of the central nervous system. Those of us who have enjoyed the privilege of testing these newer methods on a large number of hospital and private patients have also the duty of reporting the results obtained and the conclusions reached.

Omitting from present consideration all our earlier cases, we have the records of about 120 cases to form the basis of this study. It is no easy matter to arrive at just conclusions in a subject so full of pitfalls. The spontaneous remission and exacerbations of all syphilitic forms of central nervous disease make it particularly difficult to ascertain accurately the effect of any form of treatment. Hence the necessity of observing an impartial, critical attitude toward the newer remedies and methods applied to the treatment of these conditions.

We have included in the list of cases 55 cases of tabes, 20 of general paresis, 41 of cerebral and cerebrospinal lues, 3 of optic neuritis, and 2 of specific spondylitis.

Present Methods. Every patient admitted to our service in the hospital, especially if syphilitic disease of the nervous system is suspected, is subjected to a lumbar puncture for routine examination of the spinal fluid. A Wassermann test is made, using the fluid in quantities up to 1 c.c., according to the method of Hauptmann and Hoessli, and the cell count is estimated as soon as possible after the withdrawal of the spinal fluid. The Fuchs-Rosenthal chamber is used for this purpose. The globulin content is determined by the butyric acid method of Noguchi. In each case a Wassermann test of the patient's blood is also made.

We desire to sound a warning against indiscriminate lumbar puncture. After all the procedure is not indifferent or agreeable, and in every case the patient should be kept on his back for at least eighteen hours after the puncture. Intense headache and symptoms of meningeal irritation are apt to follow the operation, more especially if this precaution is not observed. We anesthetize the site of the puncture by infiltration of the region between the spinous processes with 0.5 per cent. novococain solution. In cases treated by a series of intraspinous injections the fluid is withdrawn for examination at the time of administering the serum, thus obviating the necessity of puncturing the patient merely to determine the influence of treatment.

SEROLOGICAL TECHNIQUE. In the performance of the Wassermann test we have adhered to the original technique with the following variations: (1) For the sake of economy we have reduced the total quantity by half, using 0.1 c.c. of serum as the maximum quantity instead of 0.2 c.c., as in the original test, and have reduced all the other ingredients proportionately. (2) We use as antigen the extract of normal beef or guinea-pig heart, extracted in alcohol, and fractionated by the addition of acetone according to the method of Noguchi. The acetone insoluble fraction is taken up in pure methyl alcohol and titrated for both anticomplementary (auto-inhibitory) and hemolytic properties as well as to determine its property to bind complement in the presence of syphilitic serum. We have used none but those extracts which have proved as sensitive as the alcoholic extract reinforced with cholesterin, but which showed much less tendency to hold up hemolysis in the presence of normal serum. A double quantity of the antigen extract was always used as a control and never showed any inhibitory action. The complement was titrated each time before doing the tests, care being taken to avoid an excess of complement in view of the fact that a large number of human sera contain an excess of normal antisheep amboceptor, which, in addition to the two units added in the test, is responsible for the failure to detect cases of syphilis giving only partial fixation.

We have never observed any tendency of the spinal fluid to act in an anticomplementary manner, and for this reason have not hesitated to use as much as 1 c.c. (0.5 c.c. in our system) of the fluid for the test.

All our tests are incubated for one-half hour in a water-bath at 37° C., and then are placed in the ice-box for about two or three hours before adding sheep cells. A further refinement is introduced at this point. Instead of adding two units of amboceptor with the cells or of adding sensitized sheep cells, the cell suspension alone is added and the tests placed again in the water-bath for ten minutes. At the end of this time it will be easy to note those sera that contain normal antisheep amboceptor in sufficient quantity to lake completely the control tube. To these no further hemolysin is added, while to all the other tests the usual double hemolytic dose is added. It is in this way that the presence of natural or normal sheep amboceptor is detected and the addition of an excess of hemolysin resulting often in completely laking a weakly inhibited serum is avoided.

The tests after completion were placed in the ice-box or left at cool-room temperature and the readings were taken within an hour and usually again the next morning.

TREATMENT. We have been guided in our treatment of the clinical condition by the outcome of the various biological reactions. If the examination has shown the presence of an active luetic process, intensive treatment was administered. Under such conditions it has been our routine practice to give a series of salvarsan injections intravenously at intervals of seven to ten days, the average dose being 0.25 gram to 0.4 gram. After four to six injections of salvarsan have been given the patients receive a series of intramuscular injections of salicylate of mercury in 0.5 to 1 grain doses. These injections are given weekly until from ten to fifteen injections have been administered. We have given several courses of treatment as outlined above, discharging patients for a period of three or four weeks and asking them to return for a completion of the treatment. If we have erred at all it has probably been in not pushing the treatment vigorously enough.

From our experience we are entirely disposed to agree with Dreyfus and others in holding that much more harm can be done by giving too little than too much treatment. Most observers agree that the era of excessive individual dosage has passed, and that if salvarsan is properly administered, with due regard to the patient's condition, after a careful examination of the heart, and after ascertaining that the kidneys are normal, the drug can be given repeatedly as outlined above. It is also agreed by practically all authorities, and especially by Ehrlich, that the several contra-indications detailed in the beginning of the salvarsan era have gradually been reduced in number until now it may be said that the only real contra-indications to the injection of the drug are severe renal involvement, very marked cardiac disease with insufficiency of the cardiac muscle, impending coma in diabetes or nephritis, terminal conditions which are not likely to be benefited by salvarsan, and a known intolerance of the drug.

In a very large number of cases treated with salvarsan we have observed very few untoward results. One case developed an enteritis, one a severe nephritis, another an arsenical erythema, and finally, one of our patients developed a lesion in the area supplied by the inferior cerebellar artery a number of hours after the intravenous injection of 0.3 gram salvarsan. In cases of the kind here narrated that have reacted unfavorably to the injection of the drug the question of further injections has been well considered. In most cases of this type it is possible again to inject the patient after an interval of a few weeks, and after the subsidence of untoward symptoms. Under such conditions it will be best to give not more than 0.15 gram to 0.2 gram to an adult. The injection should be given most carefully, using a concentrated solution (15 to 20 c.c. for salvarsan, 5 to 8 c.c. for neosalvarsan), more especially in cases of vascular disease.

Of the nerve recurrences (neurorecidives) which have been so frequently reported, especially by European writers, we have seen practically nothing. To be sure these are more apt to occur in the early secondary stage of syphilis, which the neurologist infrequently sees, but we question if the early neural involvement is to be attributed to salvarsan treatment properly administered. Some of these cases are surely due to early syphilitic involvement of the nervous system. We know that involvement of the cranial nerves, especially the seventh and eighth, had been described years ago as occurring toward the latter part of the secondary period by Hutchinson, Fournier, Knapp, and others, either before any treatment had been given or after treatment with any of the mercurials. These symptoms are comparable to a neuroretinitis or an iritis, and are specially frequent after insufficient sterilization of the organism by intramuscular injections of mercury or salvarsan, the remaining spirochetes localizing themselves in the poorly vascularized regions traversed by the cranial nerves mentioned above. With the adoption of the intravenous treatment, nerve recurrences have become much less frequent.

The intravenous use of old salvarsan has been so satisfactory in our experience that only recently have we made use of neosalvarsan. On account of the ease of application of this drug and the small quantity of fluid used in its preparation, and because of the less frequent incidence of immediate and remote by-effects, we now use neosalvarsan in doses of from 0.2 gram to 0.6 gram, especially in cases in which a very frequent repetition of the drug is necessary. We have thought it wise in some instances in cases in which it was doubtful if the patient was a good salvarsan risk to begin with the conservative use of neosalvarsan.

The very satisfactory results obtained by the intravenous injection of salvarsan have induced us to resort less often to the intraspinous injections of "salvarsanized serum" as proposed by Swift and Ellis.

According to our present-day conceptions the efficiency test of any antisyphilitic treatment is to be found in the improvement in the subjective and objective symptoms as well as in the change toward normal in the various biological reactions, viz., Wassermann reaction of the blood and spinal fluid, cytological count, globulin content, and, if we may be permitted to add, the luetin test.

INTRASPINOUS TREATMENT; METHODS. Aside from the fact that the intraspinous methods are all more difficult to perform than the simple intravenous injection, and surely more painful, an analysis of our cases shows that the intravenous injections alone yielded equally good results. For example, in a series of nine cases of tabes that were studied at the Montefiore Home (see Table I), the intravenous injection of salvarsan has accomplished as much for the patient as could be expected from the intraspinous injections combined with the intravenous. From this it is reasonable to conclude that the improvement is due to the intravenous medication.

TABLE I.—Cases of Advanced Tabes.

	Jan. 20 Wassermann blood	Jan. 20 cerebrospinal fluid. Wassermann cytology	Salvarsan				Wassermann blood.	Wassermann cytology. Cerebrospinal fluid.	
			Jan. 24 1914	Feb. 8 1914	Feb. 24 1914	Mar. 9 1914	April 15 1914	Apr. 18 1914	
G. D., aged 41	—	+ 80 cells	0.3	0.3	0.3	0.3	—	+ 76 cells	Pain less.
L. G., aged 31	+	+++ 21 cells	0.2	0.3	0.1	0.3	+	+ 4 cells	Pain less.
E. R., aged 48	—	++++ 108 cells	0.3	0.3	0.3	0.3	—	— 9 cells	Pain less; appears markedly impr'd.
M. N., aged 50	+	+++ 35 cells	0.3	0.3	0.3	0.3	+	— 15 cells	Pain less; appears improved.
J. C., aged 42	—	— 35 cells	0.3	0.35	0.3	...	—	— 6 cells	Pain less; impr'd general condition
D. W., aged 54	—	— 15 cells	0.3	0.3	0.3	0.4	+	— 6 cells	First relief from pain in years.
S. D., aged 64	++	+++ 75 cells	0.35	0.3	0.3	...	—	+++ 5 cells	Pain less; general condition impr.
M. G., aged 54	—	+++ 92 cells	0.3	0.4	0.3	...	...	Refused puncture	No improvement.
G. F., aged 55	—	...	0.35	0.3	0.3	...	...	Puncture impossible	Pain less.
M. F., aged 63	±	30 cells	0.4	0.3	0.4	0.45	—	Cells normal	Improved.

During the past few months we have familiarized ourselves with the injection of solutions of salvarsan and neosalvarsan in minute doses directly into the subdural space of the spinal canal. The procedure was first tried by Wechselmann and by Marinesco, and more recently has been favorably reported upon by Ravaut and others.

For intraspinous administration of these drugs a number of methods may be mentioned. The original methods of Marinesco and of Wechselmann have been modified by Ravaut, who uses a 6 per cent. solution of neosalvarsan in water. Thus if 0.6 gram of the drug were dissolved in 10 c.c. of water, each minim would contain approximately 0.003 gram of neosalvarsan. The needle is introduced as for lumbar puncture, the spinal fluid allowed to run into the funnel of the apparatus, from one to four drops of the solution are added as desired, and the mixture then allowed to run by gravity into the spinal canal. According to the method of von Schubert, 0.015 neosalvarsan is dissolved in 3 c.c. of water, and of this from 0.1 c.c. to 0.2 c.c. are added to about 3 c.c. of the spinal fluid that has been allowed to gravitate into the funnel. Gennerich avoids what he thinks is an irritative local action of the drug by dissolving 0.15 gram of neosalvarsan in 300 c.c. of water, and injects from 4 c.c. to 6 c.c. of the solution, added to 15 c.c. of the spinal fluid that has gravitated into the injecting funnel.

We have tried these methods and have recently adopted the following method: We dissolve 0.15 gram neosalvarsan in 15 c.c. of freshly distilled water or salt solution. Thus each 0.1 c.c. contains 0.001 gram of neosalvarsan. Of this solution from two to ten or more tenths of a cubic centimeter as desired are added to about 10 c.c. of the patient's spinal fluid. After gently agitating the mixture of spinal fluid and solution in the funnel the fluid is allowed to return slowly into the canal. In this way a minimal amount of fluid (foreign matter) is introduced into the canal. Should further experience prove that this solution is too concentrated it could be made up so that each cubic centimeter would contain one milligram of neosalvarsan.

For the technique of the Swift-Ellis injection of salvarsanized serum the reader is referred to the original publications. Of late some have been tempted to add a few milligrams of salvarsan to the serum before injecting according to this method.

VALUE AND DANGER OF INTRASPINOUS TREATMENT. That all intraspinous injections are not without danger to the patient is evident enough. On a number of occasions after the careful introduction into the canal of salvarsanized serum the patient required opiates to relieve the intense pain. The general condition was also much weakened and the legs partially paralyzed. One patient with early paresis within twenty-four hours after an intraspinous injection of 6 mg. of neosalvarsan developed a complete paralysis of the legs and marked paralysis of the vesical and and rectal sphincters, the symptoms persisting for three months and leading to death. In another patient with general paresis, three weeks after the sixth intraspinous injection of neosalvarsan, all of the injections having been tolerated without great discomfort, an acute ascending paralysis of the Landry type developed, and death supervened.[1] In view of these facts we have of late hesitated to urge any form of intraspinous treatment.

The various phases of the reaction of the spinal content prove, if they prove anything, that there is an active specific process going on within the cerebrospinal system. The injection of salvarsanized serum is an ingenious and fascinating proposition for which Swift and Ellis deserve great credit, and yet before accepting this method as one of value in the treatment of syphilis of the nervous system the following points should be considered.

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[1] Gennerich and others have observed irritative phenomena of lesser degree, such as weakness of the vesical and anal sphincters, shooting pains and areas of anesthesia after intraspinous injections of neosalvarsan in spite of most careful technique

It is of the utmost importance to establish the presence of salvarsan or of free arsenic in the blood of patients treated by intravenous injection in order to determine if the use of the so-called salvarsanized serum is based upon rational grounds. It seemed to us that blood withdrawn three-quarters of an hour after an intravenous injection would have to depend for whatever efficiency might be attributed to it upon the presence of the salvarsan itself, since in the short interval (three-quarters of an hour) elapsing between the injection of the drug and the withdrawal of the blood, the organism could not possibly elaborate any form of protective bodies.

We are deeply indebted to Prof. Benedict, of the Cornell Medical School, who made an analysis of ten different specimens of blood which were obtained fifteen to forty-five minutes after intravenous injection of salvarsan, with a view of determining whether or not arsenic was present in appreciable quantities. He was able to detect only 0.00004 gram to 0.0001 gram of metallic arsenic in 20 c.c. of whole blood.

By a simple calculation we have determined that a man weighing about one hundred and fifty pounds, and having a total blood volume of about eight pounds (one-nineteenth of the total weight), if injected with 0.4 gram of salvarsan would have in every cubic centimeter of his blood immediately after the injection, before elimination or fixation by the body cells began, about 0.0001 gram of salvarsan. This is the maximum amount that Benedict has shown to be present in 20 c.c. of whole blood. Thus it is apparent from the analyses of blood taken within three-quarters of an hour after the injection of salvarsan, that the arsenic is not free in the blood-stream, but is probably bound by the receptors of the body cells. Whence it follows that the serum obtained from the blood withdrawn must depend for its efficacy, if it be at all curative, upon some other factor, which has as yet not been determined. If this action depends upon the presence of antibodies in the blood, it would be much more rational to withdraw the blood a day or more after the intravenous injection.

It can be stated also on the authority of Prof. Benedict that from an analysis of four specimens of spinal fluid withdrawn twenty-four hours after an intravenous injection of salvarsan (0.4 gram) the spinal fluid contains free arsenic in about one-sixth to one-tenth the concentration in the whole blood. This is a striking fact and is contrary to the usual belief that none of the drug administered intravenously finds its way into the spinal canal.

It would seem to be proved then that since the blood-serum, which is about one-third the whole blood volume, contains only an infinitesimal trace of arsenic after an intravenous injection of the drug, that the serum as diluted (40 per cent. to 50 per cent.) for intraspinous administration is not truly salvarsanized, and that it contains no more arsenic than does the cerebrospinal fluid after simple intravenous injection. As a matter of fact the spinal fluid actually contains more arsenic than was found to be present in the "salvarsanized" serum, diluted, as used for intraspinous injection. Evidently the recorded biological effects of salvarsanized serum must be due to other coincidental factors, possibly to the intravenous injection of salvarsan and the repeated lumbar puncture.

It is of some interest in this connection to note that in one case (see Table II) the injection of non-salvarsanized (normal) serum reduced the cell count from 302 to 32 cells per cubic millimeter, while the Wassermann reaction remained strongly positive from beginning to end. More recently Dr. Mitchell (in a paper presented before the American Neurological Association) has shown that a similar reduction can be obtained by lumbar puncture frequently repeated.

TABLE II.

J. C., aged 45. Probably general paresis with optic atrophy (blindness).

Blood.	Cerebrospinal fluid.	
Wassermann, +++ March 4, 1914.	Wassermann, ++++ April 11, 1914.	30 c.c. serum intraspinous April 11, 1914.
	Wassermann, ++++ 140 cells c.mm. April 17, 1914.	30 c.c. serum intraspinous April 17, 1914.
	Wassermann, ++++ 128 cells c.mm. April 24, 1914.	30 c.c. serum intraspinous April 24, 1914.
	Wassermann, ++++ 32 cells c.mm. April 30, 1914.	30 c.c. serum intraspinous April 30, 1914.

12.5 c.c. blood-serum diluted with 17.5 normal saline and prepared according to Swift-Ellis method. Serum was obtained from a non-syphilitic patient with negative Wassermann and who had not received salvarsan.

IMPORTANCE OF BIOLOGICAL REACTIONS. Another question which arises in connection with this entire subject is whether a high cell count is a necessary accompaniment of a luetic process and whether the reduction in the number of the cells really is a distinct advantage to the patient and evidence of a change in the basic conditions underlying the morbid process. It is very evident that there is no correspondence between the change in the cell count and the change in the patient's subjective or objective symptoms. Frequently the cell count is reduced but the positive Wassermann test in the spinal fluid persists and is much more difficult to influence, if, indeed, it can be influenced at all in many cases. In cases of tabes both with and without active treatment we have often found a surprisingly low cell count or even a normal fluid in spite of the persistence of all the clinical features of the case. Then as tabes advances toward its last degenerative stages, there is in most cases a gradual, spontaneous diminution of all the biological phenomena, until finally all the reactions in the spinal fluid may become negative. In a gentleman we have been observing on and off for the past fifteen years, who has an ataxic paraplegia of specific origin, the cell count has been easily reduced to three cells per cubic millimeter by a series of three intravenous salvarsan injections. With this eminently satisfactory condition of the spinal fluid there has been, however, absolutely no improvement in the clinical symptoms. In another case of Erb's type of spinal syphilis the cell count was reduced from 88 cells to 10 cells, and the Wassermann reaction in the spinal fluid became negative, after five injections of salvarsan, but there was not the slightest change in the clinical symptoms. In still another case, though all the reactions became negative in the spinal fluid, the Wassermann remained positive in the blood, and the clinical symptoms were progressive.

We therefore question whether we are not making too much ado over the mere reduction of cells in the chronic cases of central nervous diseases. Where there is a high cell count, and particularly in the more acute luetic processes of the cerebrospinal system, there is no question of the advisability, by all possible means, of attempting to reduce the cell count. But the cell count is merely evidence of the presence of an inflammatory process, and in our enthusiasm over examinations of the spinal fluid do not let us lose sight of the patient.

We have already intimated that there is often very little correspondence between the change in the reactions in the spinal fluid and the change in the clinical symptoms; so let us consider carefully what the general effect of treatment has been on the clinical course of the various classes of cases encountered.

EFFECT OF TREATMENT. 1. As regards *tabes dorsalis:* The most striking effect of the intravenous salvarsan treatment in this condition has been that it has changed what was called a progressive locomotor ataxia into a non-progressive disease in most cases. It has been surprising to notice, particularly in private cases, how little the disease has progressed during several years of observation. In almost every instance the patient has declared that the treatment was doing him good. In the cases treated at the Montefiore Home, all of whom had been under observation for a number of years, under various forms of treatment, and most of whom were very skeptical as to the value of any new form of treatment suggested, the marked subjective improvement was readily acknowledged after salvarsan treatment.

Most of the patients at this institution were constantly receiving the analgesic drugs to reduce the terrific pain incident to the disease before salvarsan treatment was begun. That this marked betterment in the subjective state of the patient means much in so chronic a disease as tabes goes without saying. While the subjective improvement has been most marked, we have not seen what has been reported by some observers, viz., a change in the cardinal symptoms of the disease. We have not observed a permanent return of the pupillary reflexes nor of the knee-jerk or Achilles reflex. Patients in whom a return of the pupillary function or of the deep reflexes have been observed could, in our opinion, better be designated as cases of cerebrospinal lues of the tabetic type. While we can well claim that the progress of the disease has been stayed in many instances, yet we have had several rather striking experiences tending to show that in spite of early and intensive treatment the progress of an impending tabes could not be averted. Thus a gentleman whose only symptom for many years was an Argyl-Robertson pupil received twelve injections of salvarsan intravenously and innumerable injections of mercury, in spite of which the knee-jerks are growing less lively and lightning pains are making their appearance. A full-fledged tabes will soon be in evidence in spite of all treatment.

If we except the discomfort caused by lumbar puncture and the rather frequent increase in the lightning pains following salvarsan injections for a brief period there is no reason why salvarsan should not be given in every case of this type of disease, no matter at what stage the patient may come under observation, barring, of course, the very terminal period. Years ago one of us had occasion to give anatomical evidence of the fact that there was an active specific process in the bloodvessels of the cord in tabes dorsalis. The studies of the cerebrospinal content together with the anatomical and pathological studies, particularly of French observers, and the more recent findings of the presence of the Spirocheta pallida in the cord of tabic patients by Noguchi leave no doubt whatever that tabes is a syphilitic affection, and that only in its later stage can it be considered a parasyphilitic disease. The effect which salvarsan injections have upon the specific process in the spinal meninges is no doubt largely responsible for the marked subjective improvement of patients suffering from locomotor ataxia. But in our enthusiasm over salvarsan treatment, other methods should not be neglected. We wish to emphasize at this point the importance of combining salvarsan injections with the use of mercury, preferably by injections of an insoluble salt. The methods of Fränkel and Förster also should not be neglected. While arrested cases of tabes were occasionally observed before the salvarsan era it must be emphasized that they were not so frequent as they are now under the methods of treatment outlined.

2. As regards *cerebral and cerebrospinal syphilis*, including cases of chronic headache, ophthalmoplegia, and particularly hemiplegia,

it should be noted that the improvement after salvarsan treatment has been most satisfactory. Headache and ocular palsies, and even specific spondylitis, have disappeared more rapidly than under any previous form of treatment. That recovery is more rapid and more complete in hemiplegia we have also been able to record. Little more need be said on this subject than that in these cases the syphilitic process is an active one affecting the bloodvessels and the meninges chiefly, and for this reason, it may be, the salvarsan has been more effective.

We desire also to refer to several cases of optic neuritis of distinctly specific origin which we have had occasion to observe. Inasmuch as there has been at all times considerable fear of active antiluetic treatment in cases of optic neuritis, it is particularly important to emphasize the fact that energetic salvarsan treatment has been productive of excellent results, and what was feared to be a most serious condition of the optic nerves has been recovered from under this treatment. The following case in point is cited:

B. R., aged twenty-five years, single, admitted to hospital September 1, 1912. Had chancre in May, 1912. One intravenous injection of salvarsan in June followed by injections of mercury. In the beginning of August began to suffer from headaches and vomiting. About the middle of the month he noted that his right arm was becoming weak and that his eyesight was failing. His condition became progressively worse and diplopia developed. After admission to the hospital he had convulsions, affecting principally the left side. Mental state confused. Rigidity and retraction of head. Kernig's sign present. Examination of the fundi showed bilateral choked disk of three to four diopters and hemorrhage and exudate in the disk and macular region. He was treated as follows:

CASE.—B. R.

September 1, 1912. Salvarsan, 0.3. Wassermann +, blood and spinal fluid.

September 10, 1912. Salvarsan, 0.3.

September 17, 1912. Salvarsan, 0.3.

September 27, 1912. Salvarsan, 0.3.

October 4, 1912. Discharged. Optic neuritis much improved.

April 7, 1913. Readmitted. Wassermann weakly + in blood; positive in spinal fluid. 25 lymphocytes per c.mm.

May 6, 1913. Salvarsan, 0.3. Wassermann + spinal fluid. 80 cells per c.mm.

May 22, 1914. Wassermann: Negative in blood and spinal fluid. 2 cells per c.mm. Globulin: negative.

Received fourteen injections of salvarsan 0.3 to 0.4 gram and a number of injections of mercury salicylate.

At present his fundi show a postneuritic atrophy, but he has 20/20 vision in one eye and 20/30 vision in the other. There are no symptoms of any other organic lesion.

We have also had cases of tabes with optic atrophy in which the atrophy has progressed in spite of salvarsan treatment; but cases of this type should not be held to militate against the administration of salvarsan in active optic neuritis of syphilitic origin. That some such cases have gone on to blindness is unfortunately true, but however inclined to pessimism we may be, we cannot attribute such blindness to the salvarsan, nor are we willing to admit that the loss of vision and complete blindness were hastened by the use of the drug.

Here is a second case in point:

L. D., aged twenty years. Admitted to the hospital in April, 1913. She gave a history of severe headaches, vomiting, failing vision, and convulsions of Jacksonian type. Examination revealed well-marked, bilateral choked disks; Wassermann reaction negative in both blood and spinal fluid; cells only slightly increased. Salvarsan 0.25 gram given without relief. Exploratory craniotomy then performed. No tumor found, but the meninges appeared to be thickened and the seat of a chronic inflammatory process. Following the operation there was relief of symptoms until August, when she was readmitted because of the reappearance of the headaches and convulsions. The increase of cells in the spinal fluid then indicated a syphilitic process, and salvarsan was continued as shown in the case of B. R., with good effect.

It is interesting to note the increase in the cells of the spinal fluids before the Wassermann became positive, and the appearance of the reaction in the blood and spinal fluid after the administration of a considerable quantity of salvarsan. This is an example of a "provocative reaction." It is important to note that an examination of the blood of the father showed a positive reaction.

CASE L. D.—Cerebral lues (congenital).

April 10, 1913. Cerebrospinal fluid: Wassermann, —. Cells slightly increased.

April 11. Salvarsan, 0.25; intravenous. Symptoms pointed to neoplasm. Exploratory craniotomy.

April 23. Blood: Wassermann, —.

August 9. Cerebrospinal fluid: Wassermann, + (?); twenty-five cells.

October 4. Cerebrospinal fluid: Twenty-five cells.

October 8. Neosalvarsan, 0.45.

October 15. Salvarsan, 0.2. Cerebrospinal fluid: Wassermann, +. Pressure, 320 to 380 mm. Forty-one cells cubic millimeter.

November 11. Blood: Wassermann, —.

November 25. Salvarsan, 0.3, and intraspinous.

December 8. Cerebrospinal fluid: Wassermann, —. Ten cells. Globulin, ++.

December 8. Salvarsan, 0.3; intraspinous, 30 c.c.

February 9, 1914. Salvarsan, 0.3; intravenous. Cerebrospinal fluid: Wassermann, ++. Globulin, +. Twenty-four cells. Pressure, 400 mm.

February 14, 17, 19. Convulsions. .

March 10, 14, 18. Neosalvarsan, 0.6.

Still another patient presented diplopia and bilateral choked disks, and after receiving four injections of salvarsan intravenously made a complete recovery within a few weeks.

3. Finally, let us consider briefly the results of treatment in cases of *general paresis*. There is no longer doubt of the syphilitic nature of this disease since the discovery in the cortex of the brain by Noguchi and Moore of the Treponema pallida. And it may be that the ineffectiveness of our treatment up to date has been due to the fact that the salvarsan does not reach the organisms in sufficient concentration by our present methods of administration to destroy them, or that they are very resistant and that some other agent or method will have to be discovered potent enough to kill them. The fact remains that thus far we have been unable to cure a single paretic, nor are we inclined to the belief that anyone has effected a cure in an undoubted case of general paresis.

We have succeeded in arresting the disease in its early stages, temporarily in a few cases, by giving frequent doses of salvarsan intravenously. In one case of taboparesis of long duration in which the patient had developed well-marked delusions of grandeur with maniacal excitement, incontinence of urine and feces, and had a large bed-sore, the effect of the intravenous administration of the drug was truly marvellous. But it must be recorded that in the earlier period of his disease the use of mercurial injections alone had been followed by a remission. The occurrence of spontaneous remissions in this disease makes it difficult to judge of the efficacy of any form of treatment.

On the other hand we have seen some cases that not only have progressed steadily during the course of treatment, but in some instances the fatal termination seemed to have been hastened by it. We favor the use of salvarsan in general paresis, in the hope of bringing about periods of remission. Until we find an adequate substitute, salvarsan should be administered vigorously and at the earliest possible stage of the disease. The cure of general paresis is a problem for the future; its solution may be reached by further careful experimentation.

CONCLUSIONS. The most remarkable recent achievements in the treatment of syphilis of the nervous system are due to the possibilities of earlier recognition of all forms of syphilitic disease. Wherever there is a strong suspicion of syphilis, and particularly if there is corroboration of the diagnosis by examination of the blood and of the cerebrospinal content, and even in the absence of such corroboration, most intensive salvarsan treatment should be instituted. Under the ordinary precautions such treatment will do no harm and may be productive of great good. In tabes dorsalis the subjective condition of the patient can be greatly improved and the progress of the disease, checked. In all cases of cerebral and cerebrospinal lues the salvarsan treatment combined with mercury accomplishes more than we were able to accomplish by any previous methods. The intravenous injection of salvarsan has been in our opinion the most satisfactory form of treatment. The intraspinous treatment possesses no advantage over the intravenous. We have shown definitely that the "salvarsanized" serum contains an infinitesimal trace of arsenic and too little to be of any therapeutic value. The spinal fluid contains as much arsenic as does the "salvarsanized" serum. Up to the present time the results in general paresis have been the least satisfactory, but there is some reason to think that by the more careful elaboration of therapeutic methods more satisfactory results will be within reach.

CARDIAC SYPHILIS: REPORT OF CASE.[1]

By G. R. Callender, M.D.
FIRST LIEUTENANT, MEDICAL CORPS, UNITED STATES ARMY.

(Reported from the Laboratory of the United States Army General Hospital at Fort Bayard, New Mexico.)

This subject was called to the attention of the writer by the comprehensive article by Professor Harlow Brooks in the October, 1913, number of this Journal.

Shortly before the article was received here the autopsy occurred of a case of syphilitic myocarditis complicating a quiescent pulmonary tuberculosis of small degree. In view of the fact that this patient had refused all antiluetic treatment the findings histologically are thought to be of exceptional interest and worthy of report as a sequel to the paper of Professor Brooks.

Case No. 4412, admitted June 2, 1911, for pulmonary tuberculosis. Duration of disease given as seven months.

Previous History. Typhoid fever in 1889; malaria, in 1908; primary syphilis in April, 1907, for which the patient received twenty-two months' mercurial and eight months' potassium iodide treatment. No relapses. Wassermann positive in 1911.

At admission his tuberculous activity was slight and the diagnosis was active tuberculous involvement of the upper parts of both upper lobes. Tubercle bacilli were found in the sputum.

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